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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,227	03/07/2005	Koichi Saito	600630-21US (561335)	3793

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EXAMINER	
SHAFER, SHULAMITH H	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,227	SAITO, KOICHI	
	Examiner	Art Unit	
	Shulamith H. Shafer, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *20-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 6-19* is/are rejected.

7)☒ Claim(s) *3-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims

Amendments to claims:

Claims 10-14, 18, 20, 22 and 23 have been amended in communication of 25 January 2007 and the amendment made of record.

Election/Restriction:

Applicants' election (communication of 25 January 2007, in response to requirement for restriction of 21 November 2006), with traverse, of Group I, claims 1-19, drawn to a gene or nucleic acid coding for an estrogen receptor, vector comprising estrogen receptor, transformant and method for manufacturing an estrogen receptor recombinantly and further election with traverse, species B: nucleotide sequence of nucleotide numbers 74-1819 encoding a polypeptide of SEQ ID NO:4 (species 2) is acknowledged. The grounds for the traversal of the restriction requirement are: Groups II-IV contain process of use claims that are not separate and distinct from Group I. Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons: Inventions I and II-IV are related as product and process of use which are distinct inventions for reasons of record; the process claims will be considered for rejoinder upon a finding that the product claims are allowable. The claims of group I have not yet been considered on the merits; therefore applicant's arguments regarding rejoinder are not pertinent at this time.

Additionally, applicant traverses the election of species requirement, asserting that the nucleotide sequences encoding amino acid sequences are all derived from the bluegill species of fish and encode an amino acid sequence for a bluegill estrogen receptor. Applicant contends that examining all species would not constitute a serious search burden and that it is reasonable to search all sequences in one application.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons: the U.S.P.T.O considers a search for more than

one nucleic acid sequence and encoded protein a burden because the Office would have to search several different databases for the separate sequences, which would be a serious burden on the examiner and the office, especially considering the enormous numbers of sequences currently deposited in the sequence databases, which is continuing to grow at a logarithmic rate.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 1-23 are pending in the instant application. Claims 20-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-19 are under consideration to the extent they read on the elected species: a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:4, a nucleotide sequence encoding an amino acid sequence exhibiting 95% or more amino acid identity to the amino acid sequence of SEQ ID NO:4, a nucleotide sequence represented by nucleotide numbers 74-1819 of SEQ ID NO:5, the amino acid sequence of SEQ ID NO:4, or an amino acid sequence exhibiting 95% or more amino acid identity to the amino acid sequence of SEQ ID NO:4.

Information Disclosure Statement:

The Information Disclosure statements (IDS) submitted on the 7 March 2005, has been considered. Signed copy is attached.

Objections

Abstract:

The abstract of the disclosure is objected to because it is written in four paragraphs. Correction is required so that the abstract reads as a single paragraph. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. The form and legal

phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Figures:

Figure 9 is objected to because the X-axis is labeled in Japanese. Appropriate correction is required.

Claims:

Claim 4 is objected to because of the following informalities: the claim contains a grammatical error: "wherein a promoter operably linked..." should be corrected to read "wherein a promoter is operably linked....."

Claim 11 is objected to because of the following informalities: the claim contains a grammatical error: "a mammal cell" should be corrected to read "a mammalian cell".

Claims 1, 2, and 19 are objected to as reciting non-elected species. Appropriate amendment is required.

Rejections

35 U.S.C. § 101:

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, and 17-19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 2, 17 and 18 are directed to a gene or nucleotide sequence coding for an estrogen receptor. Claims 1, 2, 17 and 18, as written do not sufficiently distinguish over a gene coding for an estrogen receptor that naturally exists in cells because the claims do not particularly point out any non-naturally occurring differences between the claimed sequences and naturally occurring products. Claim 19 is directed to an estrogen receptor. The claim, as written, does not sufficiently distinguish an estrogen receptor that naturally exists in cells because the claims do not particularly point out any non-naturally occurring differences between the claimed sequences and naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. (See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of language indicating an isolated gene encoding an estrogen receptor (See MPEP 2105) and an isolated estrogen receptor.

35 U.S.C. § 112, Second Paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 6, 8-14, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 are vague and indefinite. Claim 6 recites "a viral particle containing the vector according to claim 5". Claim 5 recites "wherein the vector is a virus". It is unclear how a viral particle can contain a virus.

Claim 16 is an incomplete method claim. It is unclear what method step is intended by the recitation of "producing estrogen receptor".

Claims 8, 9, and 10 are vague and indefinite in reciting "A transformant wherein the estrogen receptor gene ....is introduced into a host cell" (Claim 8) or "wherein the vector.....is introduced into a host cell" (Claim 9) or "wherein the estrogen receptor gene is introduced into a chromosome of said host cell" (Claim 10). These claims are all directed to transformants, but they also recite method steps. It is unclear whether these claims are directed to products or methods.

Claims 8-12, as recited, read on host cells or transformants, including any eukaryotic cell. It is unclear if applicants intend isolated cells or cells transformed *in vivo*. This rejection could be overcome by adding a limitation wherein the host cells (transformants) are isolated or in culture.

Claims 11-14 are included in the rejection as dependent from rejected claims.

Claim 17 is vague and indefinite in reciting "partial nucleotide sequence". It is unclear what applicant intends by "partial nucleotide sequence". The specification has not provided a clear definition of this term; therefore the metes and bounds of the claim cannot be determined. One of ordinary skill in the art would not be able to determine which molecules are within the scope of the claims.

Claims 13, 14 and 18 are included in this rejection as dependent upon a rejected claim.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a partial nucleotide sequence of the estrogen receptor (Claim 17) wherein the partial nucleotide sequence is a nucleotide sequence coding for a ligand binding domain of the estrogen receptor (Claim 18). These claims are not enabled for the following reasons:

The specification discloses: "DNA comprising the partial nucleotide sequence of the inventive gene encoding the ligand binding domain of the estrogen receptor" includes, for example, the DNAs comprising the inventive gene-derived nucleotide sequences, containing the nucleotide sequence encoding the ligand binding domain of the estrogen receptor and not containing the nucleotide sequence encoding the DNA binding domain. Specifically, it includes, for example, the nucleotide sequences containing at least the nucleotide sequence represented by nucleotide numbers 873 to 1689 and not containing nucleotide sequence represented by nucleotide numbers 1 to 762 of SEQ ID NO: 24, and more specifically, includes the DNAs comprising the nucleotide sequence represented by nucleotide numbers 763 to 1767 of SEQ ID NO: 24. [paragraph 0106, of PGPUB 2006/0141560, the PGPUB of the instant invention]. Thus, the specification does not disclose any limiting structure, rather it teaches one exemplary sequence.

The art teaches: Estrogen receptors (ER) belong to the nuclear receptor (NR) superfamily representing a large group of transcriptional regulators with common structural organization. The structural organization of NRs consists of six functional regions showing various degrees of sequence conservation (2000. Ruff et al. Breast Cancer Res 2:353-359, page 3543, 1st column, bridging 2nd column). The ligand binding domain (LBD) is a globular domain that harbors a hormone binding site, a

dimerization interface, and a coactivator and corepressor interaction function; there is low sequence identity in LBDs of the NR superfamily (page 354, 2nd column, 2nd paragraph). The ligand binding domains of two human ER isotypes (ERα and Erβ) show only 59% sequence identity (page 354, 1st column, 1st paragraph). Thus, the art of record does not make up for the deficiencies in the specification in specifically delineating which nucleotides encode the estrogen (ligand) binding domain.

Therefore, one of ordinary skill in the art would not be able to predict which nucleotide residues a partial nucleotide sequence of the elected invention of the nucleotide sequence represented by nucleotide numbers 74 to 1719 of SEQ ID NO:5 would encompass in order to meet the required limitation of coding for a ligand binding domain of the estrogen receptor.

Due to the large quantity of experimentation necessary to determine which nucleotide residues would be required to meet the limitation of coding for a ligand binding domain of the estrogen receptor, the lack of direction/guidance presented in the specification regarding same as no reference sequences are unambiguously disclosed, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing the low sequence identity of even two isotypes of the human ER, and the breadth of the claims which fail to recite a specific nucleotide residues which encode the estrogen binding domain, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion:

Claims 1, 2, 6-19 are rejected. Claims 3-5 are objected to as dependent from rejected claims.

No claims are allowed.

Prior art made of record:

The following prior art is made of record and not relied upon is considered pertinent to applicant's disclosure. Touhata et al. (1998. Fisheries Sci. 64:131-135, cited on IDS submitted 7 March 2005, citation 2, Non-patent Literature Documents) disclose an amino acid sequence of the red seabream estrogen receptor that is 89.1% identical to SEQ ID NO:4 of the instant invention encoded by a nucleic acid sequence that is 80% identical to the nucleotide sequence comprising nucleotide numbers 74-1819 of SEQ ID NO:5 of the instant invention (see enclosed alignment and results in SCORE). However the reference does not anticipate or suggest making changes in the amino acid or nucleotide sequence to arrive at an amino acid sequence of SEQ ID NO:4 encoded by nucleotide numbers 74-1819 of SEQ ID NO:5.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

LORRAINE SPECTOR
PRIMARY EXAMINER